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Patched-2 Antibodies

RELATED APPLICATIONS

This application is a continuation of USSN 09/293,505 filed 15 April 1999, now U.S. Pat. No. 6,348,575, which claims priority under 35 U.S.C. § 119(e) to provisional application no. 60/081,884, filed 15 April 1998, all of which the entire disclosure is hereby incorporated by reference.

FIELD OF THE INVENTION

The present invention relates generally to signaling molecules, specifically to signaling and mediator molecules in the *hedgehog* (*Hh*) cascade which are involved in cell proliferation and differentiation.

BACKGROUND OF THE INVENTION

Development of multicellular organisms depends, at least in part, on mechanisms which specify, direct or maintain positional information to pattern cells, tissues, or organs. Various secreted signaling molecules, such as members of the transforming growth factor-beta (TGF- β), Wnt, fibroblast growth factors and hedgehog families have been associated with patterning activity of different cells and structures in *Drosophila* as well as in vertebrates. Perrimon, *Cell*: 80: 517-520 (1995).

Segment polarity genes were first discovered in *Drosophila*, which when mutated caused a change in the pattern of structures of the body segments. These changes affected the pattern along the head to tail axis. *Hedgehog* (*Hh*) was first identified as a segment-polarity gene by a genetic screen in *Drosophila melanogaster*, Nusslein-Volhard *et al.*, *Roux. Arch. Dev. Biol.* 193: 267-282 (1984), that plays a wide variety of developmental functions. Perrimon, *supra*. Although only one *Drosophila Hh* gene has been identified, three mammalian *Hh* homologues have been isolated: Sonic *Hh* (*Shh*), Desert *Hh* (*Dhh*) and Indian *Hh* (*Ihh*), Echelard *et al.*, *Cell* 75: 1417-30 (1993); Riddle *et al.*, *Cell* 75: 1401-16 (1993). *Shh* is expressed at high level in the notochord and floor plate of developing vertebrate embryos, and acts to establish cell fate in the developing limb, somites and neural tube. *In vitro* explant assays as well as ectopic expression of *Shh* in transgenic animals show that *SHh* plays a key role in neural tube patterning, Echelard *et al.* (1993), *supra*; Ericson *et al.*, *Cell* 81: 747-56 (1995); Marti *et al.*, *Nature* 375: 322-5 (1995); Roelink *et al.* (1995), *supra*; Hynes *et al.*, *Neuron* 19: 15-26 (1997). *Hh* also plays a role in the development of limbs (Krauss *et al.*, *Cell* 75: 1431-44 (1993); Laufer *et al.*, *Cell* 79, 993-1003 (1994)); somites (Fan and Tessier-Lavigne, *Cell* 79, 1175-86 (1994); Johnson *et al.*, *Cell* 79: 1165-73 (1994)), lungs (Bellusci *et al.*, *Develop.* 124: 53-63 (1997) and skin (Oro *et al.*, *Science* 276: 817-21 (1997)). Likewise, *Ihh* and *Dhh* are involved in bone, gut and germinal cell development, Apelqvist *et al.*, *Curr. Biol.* 7: 801-4 (1997); Bellusci *et al.*, *Dev. Suppl.* 124: 53-63 (1997); Bitgood *et al.*, *Curr. Biol.* 6: 298-304 (1996);